Complete Summary

GUIDELINE TITLE

Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Sections 6-37: chemotherapy.

BIBLIOGRAPHIC SOURCE(S)

Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Sections 6-37: chemotherapy. Bethesda (MD): Children's Oncology Group; 2006 Mar. 37 p. [191 references]

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 1.2. 2004 Mar.

** REGULATORY ALERT **

FDA WARNING/REGULATORY ALERT

Note from the National Guideline Clearinghouse: This guideline references a drug(s) for which important revised regulatory and/or warning information has been released.

- May 23, 2007, Gadolinium-based Contrast Agents: The addition of a boxed warning and new warnings about the risk of nephrogenic systemic fibrosis (NSF) to the full prescribing information for all gadolinium-based contrast agents (GBCAs).
- May 2, 2007, Antidepressant drugs: Update to the existing black box warning on the prescribing information on all antidepressant medications to include warnings about the increased risks of suicidal thinking and behavior in young adults ages 18 to 24 years old during the first one to two months of treatment.

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Late effects resulting from therapeutic exposures to chemotherapy used during treatment of pediatric malignancies. Effects include sensory (dental, ocular, otologic), reproductive (testicular, ovarian) pulmonary, urologic (urinary, renal), dermatologic, neurologic (central, peripheral, cognitive), hepatic, vascular, and skeletal sequelae; dyslipidemia; and secondary malignancies.

Note: These guidelines are intended for use beginning two or more years following the completion of cancer therapy, and provide a framework for ongoing late effects monitoring in childhood cancer survivors; however, these guidelines are not intended to provide guidance for follow-up of the pediatric cancer survivor's primary disease.

GUIDELINE CATEGORY

Counseling
Evaluation
Management
Prevention
Screening

CLINICAL SPECIALTY

Cardiology
Dentistry
Dermatology
Endocrinology
Family Practice
Gastroenterology
Internal Medicine
Nephrology
Neurology
Obstetrics and Gynecology
Oncology
Ophthalmology
Otolaryngology
Pediatrics
Pulmonary Medicine
Urology

INTENDED USERS

Advanced Practice Nurses
Dentists
Nurses
Physician Assistants
Physicians
Psychologists/Non-physician Behavioral Health Clinicians

GUIDELINE OBJECTIVE(S)

- To provide recommendations for screening and management of late effects in survivors of pediatric malignancies
- To increase quality of life and decrease complication-related healthcare costs for pediatric cancer survivors by providing standardized and enhanced follow-up care throughout the life-span that (a) promotes healthy lifestyles, (b) provides for ongoing monitoring of health status, (c) facilitates early identification of late effects, and (d) provides timely intervention for late effects

TARGET POPULATION

Asymptomatic survivors of childhood, adolescent, or young adult cancers who were treated with chemotherapy and who present for routine exposure-related medical follow-up

INTERVENTIONS AND PRACTICES CONSIDERED

Thorough history and physical examination, including targeted screening evaluations

MAJOR OUTCOMES CONSIDERED

Not stated

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

Pertinent information from the published medical literature over the past 20 years (updated as of October 2005) was retrieved and reviewed during the development and updating of these guidelines. For each therapeutic exposure, a complete search was performed via MEDLINE (National Library of Medicine, Bethesda, MD). Keywords included "childhood cancer therapy," "complications," and "late effects," combined with keywords for each therapeutic exposure. References from the bibliographies of selected articles were used to broaden the search.

NUMBER OF SOURCE DOCUMENTS

Not stated

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)
Weighting According to a Rating Scheme (Scheme Given)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

"High-level evidence" (recommendation category 1) was defined as evidence derived from high quality case control or cohort studies.

"Lower-level evidence" (recommendation categories 2A and 2B) was defined as evidence derived from non-analytic studies, case reports, case series, and clinical experience.

METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

The guidelines were scored by the multidisciplinary panel of experts using a modified version of the National Criteria: Comprehensive Cancer Network "Categories of Consensus" system. Each score reflects the expert panel's assessment of the strength of data from the literature linking a specific late effect with a therapeutic exposure, coupled with an assessment of the appropriateness of the screening recommendation based on the expert panel's collective clinical experience. "High-level evidence" (category 1) was defined as evidence derived from high quality case control or cohort studies. "Lower-level evidence" (categories 2A and 2B) was defined as evidence derived from non-analytic studies, case reports, case series and clinical experience. Rather than submitting recommendations representing major disagreements, items scored as "Category 3" were either deleted or revised by the panel of experts to provide at least a "Category 2B" score for all recommendations included in the guidelines.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

In 2002, the leadership of the Children's Oncology Group Late Effects Committee and Nursing Discipline appointed a 7-member task force, with representation from the Late Effects Committee, Nursing Discipline, and Patient Advocacy Committee. The task force was convened to review and summarize the medical literature and develop a draft of clinical practice guidelines to direct long-term follow-up care for

pediatric cancer survivors. The task force followed a modified version of the guideline development process established by the National Comprehensive Cancer Network (NCCN), integrating available literature with expert opinion using reiterative feedback loops.

The original draft went through several iterations within the task force prior to initial review. Multidisciplinary experts in the field, including nurses, physicians (pediatric oncologists and other subspecialists), patient advocates, behavioral specialists, and other healthcare professionals, were then recruited by the task force to provide an extensive, targeted review of the draft, including focused review of selected guideline sections. Revisions were made based on these recommendations. The revised draft was then sent out to additional multidisciplinary experts for further review. A total of 62 individuals participated in the review process. The guidelines subsequently underwent comprehensive review and scoring by a panel of experts in the late effects of pediatric malignancies, comprised of multidisciplinary representatives from the COG Late Effects Committee.

Revisions

In order to keep the guidelines current and clinically meaningful, the COG Late Effects Committee organized 18 multi-disciplinary task forces in March 2004. These task forces were charged with the responsibility for monitoring the medical literature in regard to specific system-related clinical topics relevant to the guidelines (e.g., cardiovascular, neurocognitive, fertility/reproductive), providing periodic reports to the Late Effects Committee, and recommending revisions to the guidelines and their associated health education materials and references (including the addition of therapeutic exposures) as new information became available. Task force members were assigned according to their respective areas of expertise and clinical interest. A list of these task forces and their membership is included in the "Contributors" section of the original guideline document. The revisions incorporated into the current release of these guidelines (Version 2.0 – March 2006) reflect the contributions and recommendations of these task forces.

All revisions proposed by the task forces were evaluated by a panel of experts, and if accepted, assigned a score (see "Rating Scheme for the Strength of the Evidence"). Proposed revisions that were rejected by the expert panel were returned with explanation to the relevant task force chair. If desired, task force chairs were given an opportunity to respond by providing additional justification and resubmitting the rejected task force recommendation(s) for further consideration by the expert panel. A total of 34 sections and 9 Health Links were added to Version 2.0 of these guidelines.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Each score relates to the strength of the association of the identified late effect with the specific therapeutic exposure based on current literature, and is coupled with a recommendation for periodic health screening based on the collective clinical experience of the panel of experts. This is due to the fact that there are no randomized clinical trials (and none forthcoming in the foreseeable future) on which to base recommendations for periodic screening evaluations in this

population; therefore, the guidelines should not be misconstrued as representing conventional "evidence-based clinical practice guidelines" or "standards of care".

Each item was scored based on the level of evidence currently available to support it. Scores were assigned according to a modified version of the National Comprehensive Cancer Network "Categories of Consensus," as follows:

1 There is uniform consensus of the panel that (1) there is high-level evidence linking the late effect with the therapeutic exposure, and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.

2A There is uniform consensus of the panel that (1) there is lower-level evidence linking the late effect with the therapeutic exposure, and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.

2B There is non-uniform consensus of the panel that (1) there is lower-level evidence linking the late effect with the therapeutic exposure, and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.

3 There is major disagreement that the recommendation is appropriate.

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

The initial version of the guidelines (Version 1.0 – Children's Oncology Group Late Effects Screening Guidelines) was released to the Children's Oncology Group (COG) membership in March 2003 for a six-month trial period. This allowed for initial feedback from the COG membership, resulting in additional review and revision of the guidelines by the Late Effects Committee prior to public release.

Revisions

All revisions proposed by the task forces were evaluated by a panel of experts, and if accepted, assigned a score (see "Rating Scheme for the Strength of the Evidence"). Proposed revisions that were rejected by the expert panel were returned with explanation to the relevant task force chair. If desired, task force chairs were given an opportunity to respond by providing additional justification and resubmitting the rejected task force recommendation(s) for further consideration by the expert panel.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

Grades of recommendations (1, 2A, 2B, 3) are defined at the end of the "Major Recommendations" field.

Note from the Children's Oncology Group and the National Guideline Clearinghouse (NGC): The *Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers* (COG LTFU) are organized according to therapeutic exposures; this guideline has been divided into individual summaries. In addition to the current summary, the following are available:

- Sections 1-2: Any Cancer Experience
- Sections 3–5: Blood/Serum Products
- Sections 38–91: Radiation
- Sections 92–106: Hematopoietic Cell Transplant
- Sections 107–132: Surgery
- Sections 133–136: Other Therapeutic Modalities
- Sections 137–146: Cancer and General Health Screening

In order to accurately derive individualized screening recommendations for a specific childhood cancer survivor using this guideline, see "Using the COG LTFU Guidelines to Develop Individualized Screening Recommendations" in the original guideline document. (Note: For ease of use, a Patient-Specific Guideline Identification Tool has been developed to streamline the process and is included in Appendix I of the original guideline document.)

Guideline Organization

The *Children's Oncology Group Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers* are organized according to therapeutic exposures, arranged by column as follows:

System	Body system (e.g., auditory, musculoskeletal) most relevant to each guideline section.
Score	Score assigned by expert panel representing the strength of data from the literature linking a specific late effect with a therapeutic exposure coupled with an assessment of the appropriateness of the screening recommendation based on collective clinical experience.
Section Number	Unique identifier for each guideline section corresponding with listing in Index.
Therapeutic Agent	Therapeutic intervention for malignancy, including chemotherapy, radiation, surgery, blood/serum products, hematopoietic cell transplant, and other therapeutic modalities.

Risk Factors	Host factors (e.g., age, sex, race, genetic predisposition), treatment factors (e.g., cumulative dose of therapeutic agent, mode of administration, combinations of agents), medical conditions (e.g., pre-morbid or co-morbid conditions), and health behaviors (e.g., diet, smoking, alcohol use) that may increase risk of developing the complication.
Highest Risk Factors	Conditions (host factors, treatment factors, medical conditions and/or health behaviors) associated with the highest risk for developing the complication.
Periodic Evaluations	Recommended screening evaluations, including health history, physical examination, laboratory evaluation, imaging, and psychosocial assessment. Recommendation for minimum frequency of periodic evaluations is based on risk factors and magnitude of risk, as supported by the medical literature and/or the combined clinical experience of the reviewers and panel of experts.
Health Counseling/ Further Considerations	***Health Links***: Health education materials developed specifically to accompany these guidelines. Title(s) of Health Link(s) relevant to each guideline section are referenced in this column. Health Link documents are included in Appendix II of the original guideline document. **Counseling**: Suggested patient counseling regarding measures to prevent/reduce risk or promote early detection of the potential treatment complication. **Resources**: See the original guideline document for lists of books and web sites that may provide the clinician with additional relevant information. **Considerations for Further Testing and Intervention**: Recommendations for further diagnostic evaluations beyond minimum screening for individuals with positive screening tests, recommendations for consultation and/or referral, and recommendations for management of exacerbating or predisposing conditions.
References	References are listed immediately following each guideline section in the original guideline document. Included are medical citations that provide evidence for the association of the therapeutic intervention with the specific treatment complication and/or evaluation of predisposing risk factors. In addition, some general review articles have been included in the Reference section of the original guideline document for clinician convenience.

Note: See the end of the "Major Recommendations" field for explanations of abbreviations included in the summary.

System = Dental
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
6	**Any Chemotherapy**	**Dental Abnormalities** Tooth/root agenesis Root thinning/shortening Enamel dysplasia	**Host Factors** Any patient who had not developed permanent dentition at time of cancer therapy **Treatment Factors** Any radiation treatment involving the oral cavity or salivary glands	**Host Factors** Younger age at treatment, especially <5 years old	**Physical** **Oral exam** (Yearly) **Screening** **Dental exam and cleaning** (Every six months)	**Health Links** **See "Patient Resources" field** Dental Health **Considerations for Further Testing and Intervention** Regular dental care including fluoride applications. Baseline panorex prior to dental procedures to evaluate root development.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Male reproductive

Scores = Alkylating agents: 1
Heavy metals: 2A
Non-classical alkylators: 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Per Evalu
7a	**Alkylating Agents** Busulfan Carmustine (BCNU) Chlorambucil Cyclophosphamide	**Gonadal dysfunction (testicular)** Delayed/arrested puberty Hypogonadism Oligospermia	**Treatment Factors** Higher cumulative doses of alkylators or combinations of alkylators Combined with radiation to:	**Host Factors** Male gender **Treatment Factors** MOPP ≥3 cycles	**History** **Puberta (onset,** **Sexual functio (erecti**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Per Evalu
	Ifosfamide Lomustine (CCNU) Mechlorethamine Melphalan Procarbazine Thiotepa **Heavy Metals** Carboplatin Cisplatin **Non-Classical Alkylators** Dacarbazine (DTIC) Temozolomide	Azoospermia Infertility	• Abdomen/pelvis • Testes • Brain, cranium (neuroendocrine axis) **Health Behaviors** Smoking **Info Link** Doses that cause gonadal dysfunction show individual variation. Germ cell function (spermatogenesis) is impaired at lower doses compared to Leydig cell (testosterone production) function. Prepubertal status does not protect from gonadal injury in males.	Busulfan $\geq$600 mg/m^2 Cyclophosphamide cumulative dose $\geq$7.5 g/m^2 or as conditioning for HCT Any alkylators combined with: • Testicular radiation • Pelvic radiation • TBI	**noctur** **emissi** **libido)** **Medica** **impacti** **sexual** **functio** (Yearly) **Physica** **Tanner** **Testicu** **volume** **Prader** **orchido** (Yearly sexually mature) **Screeni** **FSH** **LH** **Testost** (Baselin 14 **and** clinically indicate patients delayed and/or c signs ar symptor testoste deficien **Semen** **analysi** (As requ by patie for eval infertilit

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Per Evalu
					Periodic evaluati time is recomm as resu spermat can occ 10 years therapy

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Female reproductive

Scores = Alkylating agents: 1
Heavy metals: 2A
Non-classical alkylators: 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodi
7b	**Alkylating Agents** Busulfan Carmustine (BCNU) Chlorambucil Cyclophosphamide Ifosfamide Lomustine (CCNU) Mechlorethamine Melphalan Procarbazine Thiotepa **Heavy Metals** Carboplatin Cisplatin **Non-Classical Alkylators** Dacarbazine	**Gonadal dysfunction (ovarian)** Delayed/arrested puberty Premature menopause Infertility	**Treatment Factors** Higher cumulative doses of alkylators or combinations of alkylators Combined with radiation to: • Abdomen/pelvis • Lumbar or sacral spine (from ovarian scatter) • Brain, cranium (neuroendocrine axis) **Health Behaviors** Smoking **Info Link** Doses that cause gonadal	**Treatment Factors** MOPP $\geq$3 cycles Busulfan $\geq$600 mg/m^2 Cyclophosphamide cumulative dose $\geq$7.5 g/m^2 or as conditioning for HCT Any alkylators combined with: • Pelvic radiation • TBI	**History** **Pubertal tempo)** **Menstrua history** **Sexual fu (vaginal libido)** **Medicati impactin function** (Yearly) **Physical** **Tanner s** (Yearly u mature)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodi
	(DTIC) Temozolomide		dysfunction show individual variation. Females can typically maintain gonadal function at higher cumulative doses than males.		**Screenin** **FSH** **LH** **Estradiol** (Baseline **and** as cl indicated with delay irregular primary o amenorrh clinical sig symptoms deficiency

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = SMN

Scores = Alkylating agents: 1
Heavy metals: 2A
Non-classical alkylators: 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Hea Couns Furt Conside
8	**Alkylating Agents** Busulfan Carmustine (BCNU) Chlorambucil Cyclophosphamide Ifosfamide Lomustine (CCNU) Mechlorethamine Melphalan Procarbazine Thiotepa **Heavy Metals** Carboplatin Cisplatin **Non-Classical Alkylators** Dacarbazine (DTIC) Temozolomide	**Acute myeloid leukemia** **Myelodysplasia**	**Treatment Factors** Less than 10 years since exposure to agent Higher cumulative alkylator dose or combination of alkylators *Note*: Melphalan and mechlorethamine are more potent leukemogens than cyclophosphamide **Medical Conditions** Splenectomy (conflicting evidence)		**History** **Fatigue** **Bleeding** **Easy bruising** (Yearly, up to 10 years after exposure to agent) **Physical** **Dermatologic exam (pallor, petechiae, purpura)** (Yearly, up to 10 years after exposure to agent) **Screening** **CBC/differential** (Yearly, up to 10 years after exposure to agent)	**Health** **See "Pa Resourc field** Reducing Risk of S Cancers **Counsel** Counsel promptly fatigue, petechia bone pai **Conside for Furt Testing Interve** Bone ma exam as clinically indicated

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Pulmonary
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
9	**Alkylating Agents** Busulfan Carmustine (BCNU) Lomustine (CCNU)	**Pulmonary fibrosis**	**Treatment factors** Higher cumulative doses Combined with bleomycin **Medical Conditions** Atopic history **Health Behaviors** Smoking	**Treatment Factors** BCNU $\geq$600 mg/m^2 Busulfan $\geq$500 mg (transplant doses) Combined with: • Chest radiation • TBI	**History** **Cough** **SOB** **DOE** **Wheezing** (Yearly) **Physical** **Pulmonary exam** (Yearly) **Screening** **Chest x-ray** **PFTs (including DLCO and spirometry)** (Baseline at entry into long-term followup. Repeat as clinically indicated in patients with abnormal results or progressive pulmonary dysfunction.)	**Health Links** **See "Patient Resources" field** Pulmonary Health **Resources** Extensive information regarding smoking cessation is available for patients on the NCI's website: www.smokefree.gov. **Counseling** Counsel regarding tobacco avoidance/smoking cessation. Due to the potential pulmonary toxicity of this therapy, patients who desire to SCUBA dive should be advised to obtain medical clearance from a diving medicine specialist. **Considerations for Further Testing and Intervention** In patients with abnormal PFTs and/or CXR, consider repeat evaluation prior to general anesthesia. Pulmonary consultation for symptomatic pulmonary

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
						dysfunction. Influenza and pneumococcal vaccines.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Ocular
Score = 2B

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
10	**Alkylating Agents** Busulfan	**Cataracts**	**Treatment factors** Combined with corticosteroids	**Treatment Factors** Combined with cranial, orbital, or eye radiation TBI Longer interval since treatment	**History** **Visual difficulties** (Yearly) **Physical** **Eye exam (visual acuity, funduscopic exam for lens opacity)** (Yearly)	**Health Links** **See "Patient Resources" field** Cataracts **Considerations for Further Testing and Intervention** Ophthalmology consultation if problem identified. Refer patients with visual deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Urinary
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation
11	**Alkylating Agents** Cyclophosphamide Ifosfamide	**Urinary tract toxicity** Hemorrhagic cystitis Bladder fibrosis Dysfunctional voiding Vesicoureteral reflux Hydronephrosis	**Treatment Factors** Higher cumulative doses (decreased incidence with Mesna) Combined with: pelvic radiation **Health Behaviors** Alcohol use Smoking	**Treatment Factors** Cyclophosphamide dose $\geq$3 g/m^2 Pelvic radiation dose $\geq$30 Gy	**History** **Hematuria** **Urinary urgency/frequency** **Urinary incontinence/retention** **Dysuria** **Nocturia** **Abnormal urinary stream** (Yearly) **Screening** **Urinalysis** (Yearly)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = SMN
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Healt Counsel Furthe Considera
12	**Alkylating Agents** Cyclophosphamide	**Bladder malignancy**	**Treatment Factors** Combined with: pelvic radiation **Health Behaviors** Alcohol use Smoking		**History** **Hematuria** **Urinary urgency/frequency** **Urinary incontinence/retention** **Dysuria** **Nocturia** **Abnormal urinary stream** (Yearly) **Screening** **Urinalysis** (Yearly)	**Health Lin** **See "Patie Resources** Bladder Hea **Counselin** Counsel to promptly re dysuria or g hematuria **Considerat for Furthe Testing an Interventi** Urine cultur spot urine calcium/cre ratio, and ultrasound kidneys and bladder for

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Healt Counsel Furthe Considera
						patients wit microscopic hematuria (defined as RBC/HPF or least 2 occasions). Nephrology urology refe for patients culture-neg microscopic hematuria A abnormal ultrasound abnormal calcium/cre ratio. Urolo referral for patients wit culture nega macroscopi hematuria.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Urinary
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	C
13	**Alkylating Agents** Ifosfamide	**Renal toxicity** Glomerular toxicity Tubular toxicity (renal tubular acidosis, Fanconi's syndrome, hypophosphatemic rickets)	**Host Factors** Younger age at treatment Mononephric **Treatment Factors** Higher cumulative dose Combined with other nephrotoxic agents, such as:	**Host Factors** Age <5 years at time of treatment **Treatment Factors**	**Physical** **Blood pressure** (Yearly) **Screening** **BUN**	H S R fi K S K C

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	C
			• Cisplatin • Carboplatin • Aminoglycosides • Amphotericin • Immunosuppressants • Methotrexate • Radiation impacting the kidney **Medical Conditions** Tumor infiltration of kidney(s) Pre-existing renal impairment Nephrectomy	Ifosfamide dose ≥60 g/m^2 Renal radiation dose ≥15 Gy	**Creatinine** **Na, K, Cl, CO_2** **Ca, Mg, PO_4** (Baseline at entry into long-term followup. If abnormal, repeat as clinically indicated.) **Urinalysis** (Yearly)	**f T I** E su p p el w N c p h p p re in

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Auditory
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Hea Couns Furt Conside
14	**Heavy Metals** Carboplatin (in myeloablative doses only) Cisplatin **Info Link**: Patients who received carboplatin in	**Ototoxicity** Sensorineural hearing loss Tinnitus Vertigo	**Host Factors** Age <4 years at treatment **Treatment Factors** Combined with: • Cranial/ear radiation • Ototoxic drugs (e.g.,	**Host Factors** CNS neoplasm **Treatment Factors** Cumulative cisplatin dose ≥360 mg/m^2	**History** **Hearing difficulties (with/without background noise)** **Tinnitus** **Vertigo** (Yearly)	**Health L** **See "Pa Resourc field** Hearing Educatio Issues **Conside for Furt Testing**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Hea Couns Furt Conside
	non-myeloablative doses do not appear to be at risk for clinically significant ototoxicity based on results of currently available studies.		aminoglycosides, loop diuretics) **Medical Conditions** Chronic otitis Cerumen impaction Renal dysfunction	High dose cisplatin (i.e., 40 mg/m^2 per day x 5 days per course) Cisplatin administered after cranial/ear radiation Carboplatin conditioning for HCT Radiation involving ear $\geq$30 Gy	**Physical** **Otoscopic exam** (Yearly) **Screening** **Complete pure tone audiogram or brainstem auditory evoked response [BAER, ABR]** (Baseline at entry into long-term followup. If hearing loss is detected, test at least yearly, or as recommended by audiologist. For patients who also received cranial/ear radiation, test yearly after completion of therapy for 5 years [for patients <10 years old, continue yearly until age 10], then every 5 years. If clinical suspicion of hearing loss at any time, test as clinically indicated. If audiogram is inconclusive or unevaluable,	**Interve** Audiolog consultat amplifica patients progress hearing l Speech a language therapy f children hearing l Otolaryn consultat patients chronic infection cerumen impactio other anatomic problems exacerba contribut hearing l Refer pat with aud deficits t school lia commun cancer ce (psychol social wo school counselo facilitate provision educatio resource Consider specific r and/or preferent classroo seating, amplifica

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Hea Couns Furt Conside
					refer to audiologist for consideration of electrophysiologic testing e.g., OAEs.) **Info Link**: Complete pure tone audiogram should include testing of both ears: 1. Air conduction from 250 to 8000 Hz 2. Bone conduction if air conduction thresholds exceed bone by 15 dB at any frequency 3. Speech discrimination evaluation OAEs measure outer hair cell function only. Because carboplatin selectively damages inner hair cells, patients treated with carboplatin should not be evaluated with	system, other educatio assistanc indicated

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Hea Couns Furt Conside
					OAEs.	

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = PNS
Scores = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Consideration
15	**Heavy Metals** Carboplatin Cisplatin	**Peripheral sensory neuropathy** **Info Link**: Neuropathy presents as persistent effect after therapy and is typically not late in onset	**Treatment Factors** Combined with: • Vincristine • Taxanes • Gemcitabine	**Treatment Factors** Cumulative cisplatin dose $\geq$300 mg/m^2	**History** **Peripheral neuropathy** (Yearly until 2 to 3 years after therapy. Monitor yearly if symptoms persist.) **Physical** **Neurologic exam** (Yearly until 2 to 3 years after therapy. Monitor yearly if symptoms persist.)	**Health Links** **See "Patient Resources" field** Peripheral Neuropathy **Consideration for Further Testing and Intervention** Physical therap referral for patients with symptomatic neuropathy. Physical and occupational therapy assessment of hand function. Consider treatment with agent effective for neuropathic pain (e.g., gabapentin or amitriptyline).

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Urinary
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Hea Coun Fur Conside
16	**Heavy Metals** Carboplatin Cisplatin	**Renal toxicity** Glomerular injury Tubular injury Renal insufficiency	**Host Factors** Mononephric **Treatment Factors** Combined with other nephrotoxic agents such as: • Ifosfamide • Aminoglycosides • Amphotericin • Immunosuppressants • Methotrexate • Radiation impacting the kidney **Medical Conditions** Diabetes mellitus Hypertension Nephrectomy	**Treatment Factors** Cisplatin dose $\geq$200 mg/m^2 Renal radiation dose $\geq$15 Gy	**Physical** **Blood pressure** (Yearly) **Screening** **BUN** **Creatinine** **Na, K, Cl, CO_2** **Ca, Mg, PO_4** (Baseline at entry into long-term followup. If abnormal, repeat as clinically indicated.) **Urinalysis** (Yearly)	**Health** **See "Pa Resour field** Kidney I See also Kidney I **Counse** In patie salt-was tubular dysfunct educate low mag levels p coronar atheros **Conside for Furt Testing Interve** Electroly supplem patients persiste electroly wasting Nephrol consulta patients hyperte proteinu progress renal insuffici

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Cardiovascular
Score = 2B

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation
17	**Heavy Metals** Carboplatin Cisplatin	**Dyslipidemia**	**Host Factors** Family history of dyslipidemia **Medical Conditions** Overweight/Obesity		**Screening** **Fasting lipid profile** (Baseline at entry into long-term followup, then as per United States Preventive Task Force Recommendations: www.ahrq.gov/clinic/prevenix.htm)

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = CNS
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Eva
18	**Antimetabolites** Cytarabine (high dose IV) **Info Link**: High-dose IV is defined as any single dose $\geq$1000 mg/m^2.	**Neurocognitive deficits** Functional deficits in: • Executive function (planning and organization) • Sustained attention • Memory (particularly visual, sequencing, temporal memory) • Processing speed • Visual-motor integration Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change **Info Link**: Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., learning disability). Neurocognitive deficits in brain tumor survivors treated with higher doses of cranial radiation are more global (significant	**Host Factors** Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy **Treatment Factors** In combination with: • Dexamethasone • TBI • Cranial radiation • Methotrexate (IT, IO, high-dose IV) • Longer elapsed time since therapy **Info Link** Acute toxicity predominates if administered systemically as a single agent. May contribute to late neurotoxicity if combined with high dose or intrathecal methotrexate and/or cranial radiation.	**Host Factors** Age <3 years old at time of treatment Female sex Premorbid or family history of learning or attention problems **Treatment Factors** Radiation dose $\geq$24 Gy Single fraction TBI (10 Gy)	**History** **Educational vocational progress** (Yearly) **Screening** **Referral for neuropsych evaluation** (Baseline at e into long-tern follow-up, the periodically as clinically indic patients with evidence of in educational o vocational pro

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Eva
		decline in IQ). Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. New deficits may emerge over time.			

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = CNS
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluatio
19	**Antimetabolites** Cytarabine (high dose IV) **Info Link**: High-dose IV is defined as any single dose $\geq$1000 mg/m^2.	**Clinical leukoencephalopathy** Spasticity Ataxia Dysarthria Dysphagia Hemiparesis Seizures **Info Link**: Clinical leukoencephalopathy may present with or without imaging abnormalities (e.g., leukoencephalopathy, cerebral lacunes, cerebral atrophy,	**Host Factors** Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy **Treatment Factors** Combined with: • Methotrexate (IT, IO, high-dose IV) • Dexamethasone • Cranial radiation	**Treatment Factors** Radiation dose $\geq$24 Gy	**History** **Cognitive, motor, and/or sensory deficits** **Seizures** **Other neurologic symptoms** (Yearly) **Physical**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluatio
		dystrophic calcifications, mineralizing microangiopathy). Transient white matter anomalies may follow radiotherapy and high-dose chemotherapy for medulloblastoma/PNET, may mimic tumor recurrence, and signify risk of persistent neurologic sequelae. Neuroimaging changes do not always correlate with degree of cognitive dysfunction. Prospective studies are needed to define the dose/effect relationship of neurotoxic agents. *Note: new deficits may emerge over time.*			**Spasticity** **Ataxia** **Dysarthria** **Hemipare** (Yearly)

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = N/A
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
20	**Antimetabolites** Cytarabine (low dose IV) Cytarabine IO Cytarabine IT Cytarabine SQ **Info Link**: Low-dose IV is defined as any single dose	**No known late effects** **Info Link**: Acute toxicities predominate, from which the majority of patients recover without				

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
	<1000 mg/m^2.	sequelae.				

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = GI/Hepatic
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Couns Further Consid
21	**Antimetabolites** Mercaptopurine (6MP) Thioguanine (6TG) **Info Link**: Acute hepatotoxicity reported with thioguanine used in CCG 1952 (regimens B1 and B2) for ALL maintenance therapy requires longer follow-up to determine long-term sequelae. See COG Website (CCG 1952 protocol page) for updated advisories.	**Hepatic dysfunction** **VOD** **Info Link**: Acute toxicities predominate from which the majority of patients recover without sequelae. Delayed hepatic dysfunction may occur after a history of acute VOD, presenting as portal hypertension with liver biopsy indicating nodular regenerative hyperplasia, fibrosis, or siderosis.	**Medical Conditions** Viral hepatitis Previous VOD Siderosis	**Medical Conditions** Chronic viral hepatitis	**Physical** **Scleral icterus** **Jaundice** **Ascites** **Hepatomegaly** **Splenomegaly** (Yearly) **Screening** **ALT** **AST** **Bilirubin** (Baseline at entry into long-term followup. Repeat as clinically indicated.)	**Health Links** **See "Patient Res field** Liver Health **Considerations fo Further Testing a Intervention** Prothrombin time f evaluation of hepa synthetic function with abnormal live screening tests. Sc viral hepatitis in pa with persistently a liver function or an transfused prior to Gastroenterology/h consultation in pat persistent liver dys Hepatitis A and B immunization in pa lacking immunity.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Musculoskeletal
Score = 2B

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	H Cou Fu Consi
22	**Antimetabolites** Methotrexate (high dose IV) Methotrexate (low dose IV) Methotrexate IM Methotrexate PO **Info Link**: High-dose IV is defined as any single dose $\geq$1000 mg/m^2.	**Osteopenia** **Osteoporosis** Osteopenia is defined as BMD $\geq$1 and <2.5 SD below mean Osteoporosis is defined as BMD $\geq$2.5 SD below mean **Info Link**: The World Health Organization definition of osteoporosis in adults is based on comparison of a measured BMD of young adults at peak bone age and defined as a T-score. A T-score is the number of standard deviations the BMD measurement is above or below the mean. A T-score of $\geq$2.5 standard	**Host Factors** Both genders are at risk **Treatment Factors** Corticosteroids Cranial radiation HCT/TBI **Medical Conditions** Growth hormone deficiency Hypogonadism/delayed puberty Hyperthyroidism **Health Behaviors** Inadequate intake of calcium and vitamin D Lack of weight bearing exercise Smoking Alcohol use	**Host Factors** Older age at time of treatment **Treatment Factors** Methotrexate cumulative dose $\geq$40 gm/m^2 Prolonged corticosteroid therapy (e.g., for chronic GVHD)	**Screening** **Bone density evaluation (DEXA or quantitative CT)** (Baseline at entry into long-term followup. Repeat as clinically indicated.) **Info Link**: The optimal method of measuring bone health in children is controversial. Existing technologies have limitations. DEXA provides an estimate of total bone mass at a given site. Quantitative CT provides distinct measures of trabecular and cortical bone	**Health** **See "H Resou field** Bone H **Resou** Nation Osteop Founda Websit www.n **Consi for Fu Testin Interv** Nutriti supple cases osteop unresp behavi dietary manag Calciu 1500 m plus R vitami caution regard calciu supple in pati history lithiasi Treatm

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	H Cou Fu Consi
		deviations BELOW the mean is consistent with a diagnosis of osteoporosis. T-scores are not appropriate to assess skeletal health in pediatric patients who have not achieved peak adult bone mass. Instead, pediatric BMD reference data sets calculate Z-scores based on age and gender. A Z-score is the number of standard deviations the measurement is above or below the AGE-MATCHED MEAN BMD. There are no defined standards for referral or treatment of low BMD in children.			dimension and density.	exacer predis condit hormo replac therap hypog growth deficie correc chroni metab acidos could bone l Endoc consul patien osteop histor multip fractu pharm interv (e.g., bispho calcito selecti estrog recept modul

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Urinary
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Co
23	**Antimetabolites** Methotrexate (high dose IV) Methotrexate (low dose IV) Methotrexate IM Methotrexate PO **Info Link**: High-dose IV is defined as any single dose $\geq$1000 mg/m^2.	**Renal toxicity** **Info Link**: Acute toxicities predominate, from which the majority of patients recover without sequelae	**Host Factors** Mononephric **Treatment Factors** Combined with other nephrotoxic agents such as: • Cisplatin/carboplatin • Ifosfamide • Aminoglycosides • Amphotericin • Immunosuppressants • Radiation impacting the kidney **Medical Conditions** Diabetes mellitus Hypertension Nephrectomy	**Treatment Factors** Treatment before 1970	**Physical** **Blood pressure** (Yearly) **Screening** **BUN** **Creatinine** **Na, K, Cl, CO_2** **Ca, Mg, PO_4** (Baseline at entry into long-term followup. If abnormal, repeat as clinically indicated.) **Urinalysis** (Yearly)	**He** **Se Re fie** Kid Se Kid **Co fo Te In** Ne co pa hy pr pr re ins

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = GI/Hepatic
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Couns Further Consid

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Couns Further Consid
24	**Antimetabolites** Methotrexate (high dose IV) Methotrexate (low dose IV) Methotrexate IM Methotrexate PO **Info Link**: High-dose IV is defined as any single dose $\geq$1000 mg/m^2.	**Hepatic dysfunction** **Info Link**: Acute toxicities predominate, from which the majority of patients recover without sequelae	**Treatment Factors** Abdominal radiation **Medical Conditions** Viral hepatitis	**Treatment Factors** Treatment before 1970 **Medical Conditions** Chronic viral hepatitis	**Physical** **Scleral icterus** **Jaundice** **Ascites** **Hepatomegaly** **Splenomegaly** (Yearly) **Screening** **ALT** **AST** **Bilirubin** (Baseline at entry into long-term follow-up. Repeat as clinically indicated.)	**Health Links** **See "Patient Res field** Liver Health **Considerations f Further Testing a Intervention** Prothrombin time evaluation of hepa synthetic function with abnormal live screening tests. Sc viral hepatitis in pa with persistently a liver function or ar transfused prior to Gastroenterology/ consultation in pat persistent liver dys Hepatitis A and B immunization in pa lacking immunity.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = CNS
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Eva
25	**Antimetabolites** Methotrexate (high dose IV) Methotrexate IO Methotrexate IT	**Neurocognitive deficits** Functional deficits in: • Executive	**Host Factors** Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed	**Host Factors** Age <3 years old at time of treatment	**History** **Educational vocational progress** (Yearly)

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Eva
	Info Link: High-dose IV is defined as any single dose ≥1000 mg/m^2.	function (planning and organization) • Sustained attention • Memory (particularly visual, sequencing, temporal memory) • Processing speed • Visual-motor integration Learning deficits in math and reading (particularly reading comprehension) Diminished IQ Behavioral change **Info Link**: Neurocognitive deficits in survivors of leukemia and lymphoma are more frequently related to information processing (e.g., learning disability). Neurocognitive deficits in brain tumor survivors treated with higher doses of cranial radiation are more global (significant decline in IQ). Extent of deficit depends on age at treatment, intensity of treatment, and time since treatment. New	therapy **Treatment Factors** In combination with: • Dexamethasone • TBI • Cranial radiation • Cytarabine (high-dose IV) Longer elapsed time since therapy	Female sex Premorbid or family history of learning or attention problems **Treatment Factors** Radiation dose ≥24 Gy Single fraction TBI (10 Gy)	**Screening** **Referral for neuropsych evaluation** (Baseline at e into long-tern follow-up, the periodically as clinically indic patients with evidence of in educational o vocational pro

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Eva
		deficits may emerge over time.			

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = CNS
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluatio
26	**Antimetabolites** Methotrexate (high dose IV) Methotrexate IO Methotrexate IT **Info Link**: High-dose IV is defined as any single dose $\geq$1000 mg/m^2.	**Clinical leukoencephalopathy** Spasticity Ataxia Dysarthria Dysphagia Hemiparesis Seizures **Info Link**: Clinical leukoencephalopathy may present with or without imaging abnormalities (e.g., leukoencephalopathy, cerebral lacunes, cerebral atrophy, dystrophic calcifications, mineralizing microangiopathy). Transient white matter anomalies may follow radiotherapy and high-	**Host Factors** Younger age at treatment CNS leukemia/lymphoma Relapsed leukemia/lymphoma treated with CNS-directed therapy **Treatment Factors** In combination with: • Cytarabine (high-dose IV) • Dexamethasone • Cranial radiation	**Treatment Factors** Radiation dose $\geq$24 Gy	**History** **Cognitive, motor, and/or sensory deficits** **Seizures** **Other neurologi symptoms** (Yearly) **Physical** **Spasticity** **Ataxia** **Dysarthri** **Hemipare**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluatio
		dose chemotherapy for medulloblastoma/PNET, may mimic tumor recurrence, and signify risk of persistent neurologic sequelae. Neuroimaging changes do not always correlate with degree of cognitive dysfunction. Prospective studies are needed to define the dose/effect relationship of neurotoxic agents. *Note: new deficits may emerge over time.*			(Yearly)

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = SMN
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
27	**Anthracycline Antibiotics** Daunorubicin Doxorubicin Epirubicin Idarubicin Mitoxantrone* *Although Mitoxantrone technically belongs to the anthracenedione class of anti-tumor antibiotics, it is related to the anthracycline	**Acute myeloid leukemia**	**Treatment Factors** Less than 5 years since exposure to agent		**History** **Fatigue** **Bleeding** **Easy bruising** (Yearly up to 10 years after exposure to agent) **Physical** **Dermatologic exam (pallor, petechiae, purpura)**	**Health Links** **See "Patient Resources" field** Reducing the Risk of Second Cancers **Counseling** Counsel to promptly report fatigue, pallor, petechiae, or bone pain **Considerations**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
	family.				(Yearly up to 10 years after exposure to agent) **Screening** **CBC/differential** (Yearly up to 10 years after exposure to agent)	**for Further Testing and Intervention** Bone marrow exam as clinically indicated

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Cardiovascular
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors
28	**Anthracycline Antibiotics** Daunorubicin Doxorubicin Epirubicin Idarubicin Mitoxantrone* *Although Mitoxantrone technically belongs to the anthracenedione class of anti-tumor antibiotics, it is related to the anthracycline family. **Info Link**: Use the following formulas to convert to	**Cardiac toxicity** **Cardiomyopathy** **Arrhythmias** **Subclinical left ventricular dysfunction** (systolic dysfunction as assessed by ECHO or MUGA) **Info Link**: Dose levels correlating with cardiotoxicity are derived from adult studies. Childhood cancer	**Treatment Factors** Combined with radiation involving the heart Combined with other cardiotoxic chemotherapy: • Cyclophosphamide conditioning for HCT • Amsacrine **Medical Conditions** Obesity Congenital heart disease Febrile illness Pregnancy **Health Behaviors**	**Host Factors** Female sex Black/of African descent Younger than age 5 years at time of treatment **Treatment Factors** Higher cumulative anthracycline doses: • Patients 18 years or older at time of

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors
	doxorubicin/daunorubicin isotoxic equivalents prior to calculating total cumulative anthracycline dose. • Epirubicin: Multiply total dose x 0.67 • Idarubicin: Multiply total dose x 5 • Mitoxantrone: Multiply total dose x 3.5 *Note: There is a paucity of literature to support isotoxic dose conversion; however, the above conversion factors may be used for convenience in order to gauge screening frequency. Clinical judgment should ultimately be used to determine indicated screening for individual patients.*	patients exhibit clinical and subclinical toxicity at lower levels. Certain conditions (such as isometric exercise, pregnancy, and viral infections) have been anecdotally reported to precipitate cardiac decompensation. Prospective studies are needed to define risk factors. *Note: Pediatric studies of anthracycline cardiotoxicity typically describe risks based on combined cumulative doses of daunomycin and doxorubicin, assuming an equivalent relative cardiotoxicity per mg dose. Idarubicin and mitoxantrone are more cardiotoxic than doxorubicin or daunorubicin on a mg per mg dose basis. In limited studies, epirubicin has similar dose equivalency to daunomycin and doxorubicin.*	Isometric exercise Smoking Drug use (e.g., cocaine, diet pills, ephedra, mahuang)	treatment: $\geq$550 mg/m^2 • Patients younger than 18 years at time of treatment: $\geq$300 mg/m^2 • Any dose in infant Chest radiation $\geq$30 Gy Longer time elapsed since treatment

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors

Recommended Frequency of ECHO or MUGA Scan

Age at Treatment*	Chest Radiation	Anthracycline Dose**	Recommended Frequency
<1 year old	Yes	Any	Every year
	No	<200 mg/m^2	Every 2 years
		≥200 mg/m^2	Every year
1–4 years old	Yes	Any	Every year
	No	<100 mg/m^2	Every 5 years
		≥100 to <300 mg/m^2	Every 2 years
		≥300 mg/m^2	Every year
≥5 years old	Yes	<300 mg/m^2	Every 2 years
		≥300 mg/m^2	Every year
	No	<200 mg/m^2	Every 5 years
		≥200 to <300 mg/m^2	Every 2 years
		≥300 mg/m^2	Every year
Any age with decrease in serial function			Every year

*Age at time of first cardiotoxic therapy (anthracycline or chest irradiation, whichever was given first)
**Based on equivalent mg of doxorubicin/daunorubicin

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Pulmonary

Scores = Interstitial pneumonitis: 1
Pulmonary fibrosis: 1
ARDS: 2B

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Cou Furth Consider
29	**Anti-Tumor Antibiotics** Bleomycin	**Pulmonary Toxicity** Interstitial pneumonitis Pulmonary fibrosis Acute respiratory distress syndrome (very rare)	**Host Factors** Younger age at treatment **Treatment Factors** Higher cumulative dose Combined with: • Busulfan • Carmustine (BCNU) • Lomustine (CCNU) **Medical Conditions** Renal dysfunction High dose oxygen support such as during general anesthesia **Health Behaviors** Smoking	**Treatment Factors** Bleomycin dose $\geq$400 U/m^2 (injury observed in doses 60 to 100 U/m^2 in children) Combined with: • Chest radiation • TBI	**History** **Cough** **SOB** **DOE** **Wheezing** (Yearly) **Physical** **Pulmonary exam** (Yearly) **Screening** **Chest x-ray** **PFTs** (including DLCO and spirometry) (Baseline at entry into long-term follow-up. Repeat as clinically indicated in patients with abnormal results or progressive	**Health Link** **See "Patie Resources'** Pulmonary H Bleomycin A **Resources** Extensive information regarding sr cessation is for patients NCI's websit www.smoke **Counseling** SCUBA divir be avoided (potential exacerbatio pulmonary f as a result c increased ox concentratic associated w underwater pressures). healthcare p of history of bleomycin t and risk of worsening fi with high ox exposure su during gene

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Cou Furth Consider
					pulmonary dysfunction.)	anesthesia. Administrati high concen of oxygen m result in chr progressive pulmonary f Counsel reg tobacco avoidance/s cessation. **Considerat Further Tes and Interv** In patients v abnormal PF and/or CXR, consider rep evaluation p general anes Pulmonary consultation patients with symptomati progressive pulmonary dysfunction. Influenza an pneumococc vaccines.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = N/A
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
30	**Anti-Tumor Antibiotics**	**No known late effects**				

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
	Dactinomycin	**Info Link**: Dactinomycin has been associated with acute VOD, from which the majority of patients recover without sequelae.				

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Musculoskeletal
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Healt Counsel Furthe Considera
31	**Corticosteroids** Dexamethasone Prednisone	**Osteopenia** **Osteoporosis** Osteopenia is defined as BMD $\geq$1 and <2.5 SD below mean Osteoporosis is defined as BMD $\geq$2.5 SD below mean **Info Link**: The World Health Organization definition of osteoporosis in adults is based on	**Host Factors** Both genders are at risk **Treatment Factors** Methotrexate Cranial radiation HCT/TBI **Medical Conditions** Growth hormone deficiency Hypogonadism/ delayed puberty Hyperthyroidism	**Host Factors** Older age at time of treatment **Treatment Factors** Glucocorticoid cumulative dose $\geq$9 gm/m^2 prednisone equivalent Dexamethasone effect is more potent than prednisone	**Screening** **Bone density evaluation (DEXA or quantitative CT)** (Baseline at entry into long-term followup. Repeat as clinically indicated.) **Info Link**: The optimal method of measuring bone health	**Health Lin** **See "Patie Resources field** Bone Health **Resources** National Osteoporos Foundation Website: www.nof.or **Considerat for Furthe Testing an Interventi** Nutritional

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counsel Furthe Considera
		comparison of a BMD of young adults at peak bone age and defined as a T-score. A T-score is the number of standard deviations the BMD measurement is above or below the mean. A T-score of ≥2.5 standard deviations BELOW the mean is consistent with a diagnosis of osteoporosis. T-scores are not appropriate to assess skeletal health in pediatric patients who have not achieved peak adult bone mass. Instead, pediatric BMD reference data sets calculate Z-scores based on age and gender. A Z-score is the number of standard deviations the	**Health Behaviors** Inadequate intake of calcium and vitamin D Lack of weight bearing exercise Smoking Alcohol use		in children is controversial. Existing technologies have limitations. DEXA provides an estimate of total bone mass at a given site. Quantitative CT provides distinct measures of trabecular and cortical bone dimension and density.	supplement cases of osteopenia unresponsiv behavioral a dietary manageme Calcium 10 1500 mg da plus RDA fo vitamin D. U caution regarding calcium supplement in patients history of re lithiasis. Treatment exacerbatin predisposin conditions (hormonal replacemen therapy for hypogonadi growth hor deficiency, correction c chronic metabolic acidosis tha could accele bone loss). Endocrine consultation patients wit osteoporosi history of multiple fractures fo pharmacolo interventio (e.g., bisphospho calcitonin, selective

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counsel Furthe Considera
		measurement is above or below the AGE-MATCHED MEAN BMD. There are no defined standards for referral or treatment of low BMD in children.				estrogen receptor modulators

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Musculoskeletal
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Heal Counse Furth Consider
32	**Corticosteroids** Dexamethasone Prednisone	**Osteonecrosis** (Avascular Necrosis) **Info Link**: Osteonecrosis typically occurs during the acute treatment phase, may progress over time or resolve. Multifocal osteonecrosis is significantly more common (3:1) than unifocal.	**Host Factors** Both genders are at risk Host polymorphisms may confer increased risk **Treatment Factors** Combined with high-dose radiation to any bone Dexamethasone effect is more potent than prednisone	**Host Factors** Age ≥10 years at time of treatment **Treatment Factors** Orthovoltage radiation (commonly used before 1970) due to delivery of greater dose to skin and bones	**History** **Joint pain** **Swelling** **Immobility** **Limited range of motion** (Yearly) **Physical** **Musculoskeletal exam** (Yearly)	**Health Li** **See "Pat Resource field** Osteonecr **Consider for Furth Testing a Interven** MRI as cli indicated patients w history suggestiv osteonecr (should b soon after

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Heal Counse Furth Consider
			Medical Conditions Sickle cell disease			symptom onset). Orthoped consultati patients w positive in and/or symptoms osteonecr Physical t evaluation non-pharmacc pain managem range of motion, strengthe stretching functional mobility).

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Ocular
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
33	**Corticosteroids** Dexamethasone Prednisone	**Cataracts**	**Treatment Factors** Combined with: • TBI • Busulfan	**Treatment Factors** TBI Cranial, orbital, or eye radiation Longer interval since treatment	**History** **Visual difficulties** (Yearly) **Physical** **Eye exam** (visual acuity, funduscopic	**Health Links** **See "Patient Resources" field** Cataracts **Considerations for Further Testing and Intervention**

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
					exam for lens opacity) (Yearly)	Ophthalmology consultation if problem identified. Refer patients with visual deficits to school liaison in community or cancer center (psychologist, social worker, school counselor) to facilitate acquisition of educational resources.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = N/A
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
34	**Enzymes** Asparaginase	**No known late effects** **Info Link**: Acute toxicities predominate, from which the majority of patients recover without sequelae				

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = PNS
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
35	**Plant Alkaloids** Vinblastine Vincristine	**Peripheral sensory or motor neuropathy** Areflexia Weakness Foot drop Paresthesias **Info Link**: Acute toxicities most commonly occur and usually resolve prior to patients entering long-term follow-up. Neuropathy can persist after treatment and is typically not late in onset.	**Treatment Factors** Combined with platinum chemotherapy, gemcitabine, or taxanes **Medical Conditions** Anorexia Severe weight loss	**Medical Conditions** Charcot-Marie-Tooth disease	**History** **Peripheral neuropathy** (Yearly, until 2 to 3 years after therapy. Monitor yearly if symptoms persist.) **Physical** **Neurologic exam** (Yearly, until 2 to 3 years after therapy; continue to monitor yearly if symptoms persist)	**Health Links** **See "Patient Resources" field** Peripheral Neuropathy **Considerations for Further Testing and Intervention** Physical therapy referral for patients with symptomatic neuropathy. Physical therapy and occupational therapy assessment of hand function. Consider treatment with an anticonvulsant effective for neuropathic pain (e.g., gabapentin and amitriptyline).

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = Cardiovascular
Score = 2A

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counseling Further Considerations
36	**Plant Alkaloids** Vinblastine Vincristine	**Vasospastic attacks** (Raynaud's phenomenon)	**Health Behaviors** Smoking Illicit drug use		**History** **Vasospasms of hands, feet, nose, lips, cheeks, or earlobes related to stress or cold temperatures** (Yearly) **Physical** **Physical exam of affected area** (As Indicated)	**Health Links** **See "Patient Resources" field** Raynaud's Phenomenon **Counseling** Counsel to wear appropriate protective clothing in cold environments and not to use tobacco or illicit drugs **Considerations for Further Testing and Intervention** Consider vasodilating medications (calcium-channel blockers, alpha blockers) for patients with frequent, severe vasospastic attacks unresponsive to behavioral management.

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

System = SNM
Score = 1

Sec #	Therapeutic Agent(s)	Potential Late Effects	Risk Factors	Highest Risk Factors	Periodic Evaluation	Health Counsel Furthe Considera
37	**Epipodophyllotoxins** Etoposide (VP16) Teniposide (VM26) **Info Link**: Administration schedules since approximately 1990 have been modified to reduce the risk of this complication.	**Acute myeloid leukemia**	**Medical Conditions** Splenectomy (conflicting evidence)	**Treatment Factors** Weekly or twice weekly administration Less than 5 years since exposure to agent	**History** **Fatigue** **Bleeding** **Easy bruising** (Yearly, up to 10 years after exposure to agent) **Physical** **Dermatologic exam (pallor, petechiae, purpura)** (Yearly, up to 10 years after exposure to agent) **Screening** **CBC/differential** (Yearly, up to 10 years after exposure to agent)	**Health Lin** **See "Patie Resources field** Reducing th Risk of Sec Cancers **Counselin** Counsel to promptly re fatigue, pa petechiae, bone pain **Considera for Furthe Testing ar Interventi** Bone marro exam as clinically indicated

Note: See a list of Abbreviations at the end of the "Major Recommendations" field.

Abbreviations

- ABR, auditory brainstem response
- ALT, alanine aminotransferase
- AST, aspartate aminotransferase
- BAER, brainstem auditory evoked responses
- BMD, bone mineral density
- BUN, blood urea nitrogen
- Ca, calcium
- CBC, complete blood count

- CCG, Children's Cancer Group
- Cl, chloride
- CNS, central nervous system
- CO_2, carbon dioxide
- COG, Children's Oncology Group
- CT, computed tomography
- CXR, chest x-ray
- DEXA, dual energy x-ray absorptiometry
- DLCO, diffusion capacity of carbon monoxide
- DOE, dyspnea on exertion
- ECHO, echocardiogram
- EKG, electrocardiogram
- FSH, follicle-stimulating hormone
- GI, gastrointestinal
- GVHD, graft versus host disease
- Gy, gray
- HCT, hematopoietic cell transplant
- HPF, high power field
- HZ, hertz
- IM, intramuscular
- IO, intraosseous
- IQ, intelligence quotient
- IT, intrathecal
- IV, intravenous
- K, potassium
- LH, luteinizing hormone
- Mg, magnesium
- MOPP, mechlorethamine/Oncovin [vincristine]/procarbazine/prednisone
- MR, magnetic resonance
- MRI, magnetic resonance imaging
- MUGA, multiple gated acquisition scan
- N/A, not applicable
- Na, sodium
- NCI, National Cancer Institute
- OAEs, otoacoustic emissions
- PFTs, pulmonary function tests
- PNET, primitive neuroectodermal tumor
- PNS, peripheral neurosensory
- PO, by mouth
- PO_4, phosphate
- RBC, red blood cell
- RDA, recommended daily allowance
- SD, standard deviaion(s)
- SMN, secondary malignant neoplasm
- SOB, shortness of breath
- SQ, subcutaneous
- TBI, total body irradiation
- VOD, veno-occlusive diseases

Definitions:

Explanation of Scoring for the Long-Term Follow-Up Guidelines

1 There is uniform consensus of the panel that (1) there is high-level evidence linking the late effect with the therapeutic exposure, and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.

2A There is uniform consensus of the panel that (1) there is lower-level evidence linking the late effect with the therapeutic exposure, and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.

2B There is non-uniform consensus of the panel that (1) there is lower-level evidence linking the late effect with the therapeutic exposure, and (2) the screening recommendation is appropriate based on the collective clinical experience of panel members.

3 There is major disagreement that the recommendation is appropriate.

Rating Scheme for the Strength of the Evidence

"High-level evidence" (recommendation category 1) was defined as evidence derived from high quality case control or cohort studies.

"Lower-level evidence" (recommendation categories 2A and 2B) was defined as evidence derived from non-analytic studies, case reports, case series, and clinical experience.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

The type of supporting evidence is identified and graded for each recommendation (see "Major Recommendations").

Although several well-conducted studies on large populations of childhood cancer survivors have demonstrated associations between specific exposures and late effects, the size of the survivor population and the rate of occurrence of late effects does not allow for clinical studies that would assess the impact of screening recommendations on the morbidity and mortality associated with the late effect. Therefore, scoring of each exposure reflects the expert panel's assessment of the level of literature support linking the therapeutic exposure with the late effect coupled with an assessment of the appropriateness of the recommended screening modality in identifying the potential late effect based on the panel's collective clinical experience.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

Potential benefits of implementing these guidelines into clinical practice include earlier identification of and intervention for late onset therapy-related complications in this at-risk population, potentially reducing or ameliorating the impact of late complications on the health status of survivors. In addition, ongoing healthcare that promotes healthy lifestyle choices and provides ongoing monitoring of health status is important for all cancer survivors.

POTENTIAL HARMS

Potential harms of guideline implementation include increased patient anxiety related to enhanced awareness of possible complications, as well as the potential for false-positive screening evaluations, leading to unnecessary further workup. In addition, costs of long-term follow-up care may be prohibitive for some patients, particularly those lacking health insurance, or those with insurance that does not cover the recommended screening evaluations.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The information and contents of each document or series of documents made available by the Children's Oncology Group relating to late effects of cancer treatment and care or containing the title "Long-Term Follow-Up Guidelines for Survivors of Childhood, Adolescent, and Young Adult Cancers" or the title "Health Link," whether available in print or electronic format (including any digital format, e-mail transmission, or download from the website), shall be known hereinafter as "Informational Content." All Informational Content is for informational purpose only. The Informational Content is not intended to substitute for medical advice, medical care, diagnosis, or treatment obtained from a physician or healthcare provider.
- *To cancer patients (if children, their parents or legal guardians)*: Please seek the advice of a physician or other qualified healthcare provider with any questions you may have regarding a medical condition and do not rely on the Informational Content. The Children's Oncology Group is a research organization and does not provide individualized medical care or treatment.
- *To physicians and other healthcare providers*: The Informational Content is not intended to replace your independent clinical judgment, medical advice, or to exclude other legitimate criteria for screening, health counseling, or intervention for specific complications of childhood cancer treatment. Neither is the Informational Content intended to exclude other reasonable alternative follow-up procedures. The Informational Content is provided as a courtesy, but not intended as a sole source of guidance in the evaluation of childhood cancer survivors. The Children's Oncology Group recognizes that specific patient care decisions are the prerogative of the patient, family, and healthcare provider.
- While the Children's Oncology Group has made every attempt to assure that the Informational Content is accurate and complete as of the date of

publication, no warranty or representation, express or implied, is made as to the accuracy, reliability, completeness, relevance, or timeliness of such Informational Content.

- No liability is assumed by the Children's Oncology Group or any affiliated party or member thereof for damage resulting from the use, review, or access of the Informational Content. You agree to the following terms of indemnification: (i) "Indemnified Parties" include authors and contributors to the Informational Content, all officers, directors, representatives, employees, agents, and members of the Children's Oncology Group and affiliated organizations; (ii) by using, reviewing, or accessing the Informational Content, you agree, at your own expense, to indemnify, defend and hold harmless Indemnified Parties from any and all losses, liabilities, or damages (including attorneys' fees and costs) resulting from any and all claims, causes of action, suits, proceedings, or demands related to or arising out of use, review or access of the Informational Content.
- Ultimately, as with all clinical guidelines, decisions regarding screening and clinical management for any specific patient should be individually tailored, taking into consideration the patient's treatment history, risk factors, co-morbidities, and lifestyle. These guidelines are therefore not intended to replace clinical judgment or to exclude other reasonable alternative follow-up procedures. The Children's Oncology Group recognizes that specific patient care decisions are the prerogative of the patient, family, and healthcare provider.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

Implementation of these guidelines is intended to standardize and enhance follow-up care provided to survivors of pediatric malignancies throughout the lifespan. Considerations in this regard include the practicality and efficiency of applying these broad guidelines in individual clinical situations. Studies to address guideline implementation and refinement are a top priority of the Children's Oncology Group (COG) Late Effects Committee, and proposals to study feasibility of guideline use in limited institutions are currently underway. Issues to be addressed include description of anticipated barriers to application of the recommendations in the guidelines and development of review criteria for measuring changes in care when the guidelines are implemented. Additional concerns surround the lack of current evidence establishing the efficacy of screening for late complications in pediatric cancer survivors. While most clinicians believe that ongoing surveillance for these late complications is important in order to allow for early detection and intervention for complications that may arise, development of studies addressing the efficacy of this approach is imperative in order to determine which screening modalities are optimal for asymptomatic survivors.

In addition, the clinical utility of this lengthy document has also been a top concern of the COG Late Effects Committee. While recognizing that the length and depth of these guidelines is important in order to provide clinically-relevant, evidence-based recommendations and supporting health education materials, clinician time limitations and the effort required to identify the specific recommendations relevant to individual patients have been identified as barriers to their clinical application. Therefore, the COG Late Effects Committee is currently

partnering with the Baylor School of Medicine in order to develop a web-based interface, known as "Passport for Care," that will generate individualized exposure-based recommendations from these guidelines in a clinician-focused format for ease of patient-specific application of the guidelines in the clinical setting. As additional information regarding implementation of the Passport for Care web-based interface becomes available, updates will be posted at www.survivorshipguidelines.org.

IMPLEMENTATION TOOLS

Chart Documentation/Checklists/Forms
Patient Resources
Resources

For information about availability, see the "Availability of Companion Documents" and "Patient Resources" fields below.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness
Staying Healthy

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Sections 6-37: chemotherapy. Bethesda (MD): Children's Oncology Group; 2006 Mar. 37 p. [191 references]

ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

2003 Sep (revised 2006 Mar)

GUIDELINE DEVELOPER(S)

Children's Oncology Group - Medical Specialty Society

SOURCE(S) OF FUNDING

This work was supported by the Children's Oncology Group grant U10 CA098543 from the National Cancer Institute.

GUIDELINE COMMITTEE

Children's Oncology Group Nursing Discipline and Late Effects Committee

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Melissa M. Hudson, MD
Vice-Chair – COG Late Effects Committee
Member, Department of Hematology-Oncology
Director, After Completion of Therapy Clinic
St. Jude Children's Research Hospital
Memphis, Tennessee

Wendy Landier, RN, MSN, CPNP, CPON®
Chair – COG Nursing Clinical Practice Subcommittee
Clinical Director - Survivorship Clinic
City of Hope Comprehensive Cancer Center
Duarte, California

Smita Bhatia, MD, MPH
Chair – COG Late Effects Committee
Professor and Chair, Division of Population Sciences
City of Hope Comprehensive Cancer Center
Duarte, California

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

All Children's Oncology Group (COG) members have complied with the COG conflict of interest policy, which requires disclosure of any potential financial or other conflicting interests.

GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Children's Oncology Group. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 1.2. 2004 Mar.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Children's Oncology Group Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following are available:

- Instructions for use. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 2.0. Children's Oncology Group. 2006 March. 6 p.
- Introductory material. Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 2.0. Children's Oncology Group. 2006 March. 9 p.
- Summary of cancer treatment. Appendix I: Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 2.0. Children's Oncology Group. 2006 March.
- Patient-specific guideline identification tool. Appendix I: Long-term follow-up guidelines for survivors of childhood, adolescent, and young adult cancers. Version 2.0. Children's Oncology Group. 2006 March.

Electronic copies: Available in Portable Document Format (PDF) from the Children's Oncology Group Web site.

PATIENT RESOURCES

In an effort led by the Nursing Clinical Practice Subcommittee, complementary patient education materials (*Health Links*) were developed and are available in Appendix II of the original guideline document. The following Health Links are relevant to this summary:

Section 6

- Dental Health

Section 7

- Male Health Issues
- Female Health Issues

Sections 8, 27, 37

- Reducing the Risk of Second Cancers

Sections 9, 29

- Pulmonary Health

Sections 10, 33

- Cataracts

Sections 11, 12

- Bladder Health

Sections 13, 16, 23

- Kidney Health
- Single Kidney Health (mononephric patients only)

Section 14

- Hearing Loss

Sections 14, 18, 25

- Educational Issues

Sections 15, 35

- Peripheral Neuropathy

Section 17

- Diet and Physical Activity

Sections 21, 24

- Liver Health

Sections 22, 31

- Bone Health

Section 28

- Heart Health

Section 29

- Bleomycin Alert

Section 32

- Osteonecrosis

Section 36

- Raynaud's Phenomenon

has been derived and prepared from a guideline for health care professionals included on NGC by the authors or publishers of that original guideline. The patient information is not reviewed by NGC to establish whether or not it accurately reflects the original guideline's content.

NGC STATUS

This NGC summary was completed by ECRI Institute on May 8, 2007. The information was verified by the guideline developer on June 11, 2007. This summary was updated by ECRI Institute on November 9, 2007, following the U.S. Food and Drug Administration advisory on Antidepressant drugs.

COPYRIGHT STATEMENT

DISCLAIMER

NGC DISCLAIMER

The National Guideline Clearinghouse™ (NGC) does not develop, produce, approve, or endorse the guidelines represented on this site.

All guidelines summarized by NGC and hosted on our site are produced under the auspices of medical specialty societies, relevant professional associations, public or private organizations, other government agencies, health care organizations or plans, and similar entities.

Guidelines represented on the NGC Web site are submitted by guideline developers, and are screened solely to determine that they meet the NGC Inclusion Criteria which may be found at http://www.guideline.gov/about/inclusion.aspx .

NGC, AHRQ, and its contractor ECRI Institute make no warranties concerning the content or clinical efficacy or effectiveness of the clinical practice guidelines and related materials represented on this site. Moreover, the views and opinions of developers or authors of guidelines represented on this site do not necessarily state or reflect those of NGC, AHRQ, or its contractor ECRI Institute, and inclusion or hosting of guidelines in NGC may not be used for advertising or commercial endorsement purposes.

Readers with questions regarding guideline content are directed to contact the guideline developer.

Date Modified: 9/22/2008


DEPARTMENT OF HEALTH & HUMAN SERVICES • USA